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EXAMINER
WOODWARD, M

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/22/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 60-66 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-59 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 60-66 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Applicant's arguments filed December 22, 1994 have been fully considered but they are not deemed to be persuasive.

The rejection of claims 60-66 under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed is withdrawn.

The rejection of claims 60-66 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn for the following reasons:

"Antigen" as a replacement for "immunogenic polypeptide" has support in the specification.

At page 3 of the '501 specification, the '534 specification, the '447 specification and page 5 of the '984 specification it is stated

> "Based on the nucleotide sequences, synthetic peptides may also be prepared."

This sentence concludes the summary of the invention section of the specification for the '501, '534, and '447 applications. From this language and the discussion which precedes it one of ordinary skill in the art would conclude that the metes and bounds of synthetic peptides would exclude those peptides made recombinantly.

Claims 60-66 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 60, 61 and 66 recite "synthetic peptide," which leads one to conclude that synthetic is a process limitation. As such it does not impart patentable distinctness to the peptide absent a demonstration that the peptide so produced is materially different either from that recombinantly produced or that which is naturally occurring. Furthermore, the recitation of polypeptides with reference to recombinantly expressed antigens of the envelope region and peptides with respect to synthetically produced antigens is suggestive that a difference exists between the two. Such a difference is nowhere set forth in the specification. Perhaps the intent was to convey a difference in size of the respective products, however, the specification does not set forth ranges for either type of antigen. However, the meaning of "synthetic peptide" could also be inclusive of in vitro translated synthetic mRNA as well as fragments of a protein obtained by chemical or enzymatic means. While the claim language and the specification suggest that recombinantly expressed polypeptides are not within the metes and bounds of "synthetic peptides" neither the claims nor the specification clearly sets forth what is.

Claims 60-66 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 60-66 are again rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Applicant is correct regarding the deposit of the lambda clone and that portion of the rejection is withdrawn.

The thrust of the rejection in the prior Office action was that it would require undue experimentation to determine which synthetic peptides would function in immunoassays for the presence of anti-HIV antibodies.

As previously set forth:

> Applicants do not provide guidance as to how to produce immunogenic portions of the envelope domain of HIV. There is no description of what regions of the envelope domain contribute to its immunogenicity nor is there description of which immunogenic domains lead to the formation of antibodies in humans infected with HIV. Presentation of the sequence of the HIV genome and examples of the expression of portions of the envelope domain are insufficient to establish that untested regions or regions smaller than those exemplified would have a reasonable expectation of being immunogenic or of being recognized by antibodies present in humans infected with HIV. The exemplified domains are starting points for trying to find out if there are smaller regions therein which have the required activity.
>
> Application SN 06/667501 sets forth the expression of the putative envelope region by COS cells infected with an expression vector containing an approximately 3300 bp KpnI-EcoRI fragment of the HIV genome. . . . Expression in COS cells was detected by immunofluorescence and there is no guidance as to how to prepare the expressed protein for use in other immunoassay formats. There is no characterization of the expressed product with regard to its molecular weight, post-translational modification, e.g. glycosylation or proteolytic cleavage, or cellular localization. Nor is it clear from the specification that the expressed material which is being recognized actually reflects recognition of envelope domains in as much as the insert contains sequences additional to the putative envelope gene. Nor does the specification set forth guidance as to what modifications to the KpnI-EcoRI fragment may be necessary in order to facilitate expression in other eukaryotic or prokaryotic expression systems.
>
> . . .
>
> The specification of SN 07/138894 and its children set forth additional specific embodiments of portions of the env domain and their expression in bacteria and yeast. However, the specification does not provide guidance as to what sub-regions of the expressed domains would have a reasonable expectation of being recognized by antibodies present in the sera of patients infected with HIV.

As originally presented the rejection concerned both recombinantly produced polypeptides and synthetic peptides as they were viewed as being

within the scope of synthetic peptide. As set forth above it would appear from the specification that applicants did not regard recombinantly expressed polyeptides as within the scope of synthetic peptides. Thus, the issue becomes whether or not the specification provides an enabling disclosure for the production of synthetic peptides which are not produced by recombinant means.

At page 9, second paragraph of Paper No. 11 (December 22, 1994) applicants point to several passages in the instant specification as providing an enabling disclosure for the production of immunogenic portions of the envelope domain of HIV. In reviewing each of the cited passages the examiner notes that each is directed to a recombinantly expressed antigen absent any mention of its synthetic equivalent and therefore do not constitute an enabling disclosure for synthetic peptides.[1]

Applicants' traversal of the enablement rejection with regard to synthetic peptides relies on the argument that the prior art teachings of Geysen et al. (1984) would have been known to the person of ordinary skill in the art and that Geysen et al. (1984) demonstrates that it was routine experimentation to obtain smaller antigenic fragments than those specifically disclosed in the specification.

This line of argument is not persuasive as there is no guidance in the specification which leads to Geysen et al. or any reference to methods of

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[1] At page 10 of Paper No. 11 (December 22, 1994) applicants assert that the immunofluorescence experiments demonstrate that the envelope domain was expressed because the antibody used was directed to envelope antigens. However, there is nothing in the specification which suggests that such a specific antibody was employed. Nor is there any evidence in the prior art which would suggest that such antibody preparations were routinely made or available. In fact, at the time of filing the actual envelope proteins of the virus had not been disclosed in the scientific literature. It was hypothesized from comparisons with HTLV-I and II where the envelope domains would be, however, as it turns out the envelope proteins of HIV are quite different.

determining antigenic peptides in the instant or any previously filed specification. The Geysen et al. publication was a seminal publication which has ultimately lead to strategies for obtaining antigenic epitopes, however, it cannot be concluded solely from its teachings that the procedure would work for a structurally unrelated protein, i.e., there is no reason to believe a priori that the antigenic structure of a viral capsid protein is predictive of the antigenic structure of a retroviral envelope protein, particularly when the structure of the retroviral envelope protein was unknown. At a minimum no argument has been presented that it is reasonable to expect that the antigenic repertoire of a viral capsid protein which associates with other proteins to form a capsid would be expected to be similar to what would be expected to be a membrane glycoprotein.

Even if Geysen et al. represented an art recognized experimental procedure applicants' traversal would not be persuasive because what is set forth in Geysen et al. is a technique to begin to assemble those peptides which could be used in immunoassays. It is set forth in Figure 2 and at page 4001, left hand column that the response of any one individual is idiosyncratic, i.e., that any particular individual shows an individual specific response. Thus, one cannot reasonably expect that a peptide will be as effective as the entire protein nor that all individuals will produce antibodies which recognize a single peptide.

Moreover, Geysen et al. does not address how to produce synthetic peptides which possess conformational, as opposed to linear epitopes. Given that the immune system is exposed to intact virus and virally infected cells it is expected that the predominant response would be to conformational rather than linear epitopes and that one in making synthetic peptides would seek to produce such conformational epitopes. However, the specification is completely silent in

this regard.

In as much as the specification discloses no range of sizes for the synthetic peptides the claims are considered to have within their scope peptides which would be equivalent in size to the envelope domain. But, while the Merrifield technique for solid phase synthesis of peptides was art recognized there is no suggestion that large peptides, e.g. greater than 100 amino acids, could be reliably produced. Nor that one could stitch together smaller peptide fragments which then properly folded into a native conformation.

Claims 60-66 are again rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 5,156,949. Although the conflicting claims are not identical, they are not patentably distinct from each other because the difference between the claimed inventions is the manner in which the antigen is produced. However, there has been no showing that the process of producing the antigens in question in anyway leads to a materially or functionally different product.

The examiner notes applicants' intent to file a Terminal Disclaimer.

The specifications of the '501 and '534 applications do not provide support for the invention as is now claimed.

The sole reference to synthetic polypeptides in the '501 and '534 specifications occurs in the summary of the invention section at the close of a paragraph directed to the recombinant expression of polypeptides for use as vaccines. The instant claims are directed to immunoassays employing and solid supports upon are immobilized synthetic peptides from the envelope domain of HIV. Nowhere in the '501 and '534 specifications is reference made to the use

of synthetic peptides in immunoassays. On this basis alone the instant claims would be entitled to a filing date no earlier than that of SN 06/773447 which is September 6, 1985.

However, in view of the rejection made under 35 U.S.C. §112, first paragraph above the claims are accorded the filing date of the instant application.

Claims 60-66 are again rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Chang et al. (US Patent 4,774,175). See for example claims 2-15.

Claims 60-66 are again rejected under 35 U.S.C. § 102(b) as being anticipated by Cosand (US Patent 4,629,783). Cosand describes peptides from the env domain of HIV and their use in solid phase immunoassays for the detection of antibodies present in the sera of patients infected with HIV.

Applicants traversal of these rejections is that they are moot because they do not predate the '501 application. However, as set forth above the instant claims are not entitled to the filing date of either the '501 or '534 application. It is also noted with regard to Chang et al. that it is deemed anticipatory despite the fact that the Chang et al. peptide is produced recombinantly as applicant has not shown that this apparent process limitation in anyway materially effects the product.

The following rejections are provisional in that they are applicable should applicants demonstrate that the specification of 06/773447 is enabling for the production of synthetic peptide antigens.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 60-66 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Chang et al. (US Patent 4,774,175).

Claims 60-66 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Cosand (US Patent 4,629,783).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Woodward whose telephone number is (703) 308-3890.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989).

The CM1 Fax Center number is (703) 305-3014.

MICHAEL P. WOODWARD
PRIMARY EXAMINER
GROUP 1800

March 18, 1995